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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Gardere Wynne Sewell LLP
Suite 3000
1601 Elm Street
Dallas, TX 75201

EXAMINER

HADDAD, MAHER M

ART UNIT PAPER NUMBER

1644

DATE MAILED: 01/14/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

09/801,348

Applicant(s)

HARPER ET AL.

Examiner

Maher M. Haddad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-23 and 27-30 is/are pending in the application.
- 4a) Of the above claim(s) 27-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-12 and 14-23 is/are rejected.
- 7) ☒ Claim(s) 13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Claims 10-23 and 27-30 are pending.
2. The new Restriction Requirement set below:
 - I. Claims 10-23, drawn to an isolated nucleic acid of SEQ ID NO: 54, a vector and a host cell, classified in Class 536, subclasses 23.4 and 23.5 and Class 435, subclass 320.1 and 325.
 - II. Claims 10-23, drawn to an isolated nucleic acid of SEQ ID NO: 56, a vector and a host cell, classified in Class 536, subclasses 23.4 and 23.5 and Class 435, subclass 320.1 and 325.
 - III. Claims 27-30, drawn to a fusion protein comprising a portion of the gene SEQ ID NO: 54 and a non-functional active F-Box domain protein sequence, classified in Class 530, subclasses 352.
 - IV. Claims 27-30, drawn to a fusion protein comprising a portion of the gene SEQ ID NO: 56 and a non-functional active F-Box domain protein sequence, classified in Class 530, subclasses 352.
3. During a telephone conversation between the previous Examiner, Ruixiang Li and Thomas C. Wright on 11/20/02 a provisional election was made with traverse to prosecute the invention of Group I, claims 10-23, drawn to a nucleic acid segment of SEQ ID NO: 54, vectors and host cells. Affirmation of this election must be made by applicant in replying to this Office action.

Applicant's traversal is on the grounds that no serious burden on the examiner has been shown and the Examiner failed to explain whether there is a separate classification of the separate nucleic acid/amino acid sequences. Applicant further argues that the Examiner failed to establish separate fields of searching would be required. This is not found persuasive because the specific nucleic acids of SEQ ID Nos: 54 and 56 and a fusion protein comprising a portion of the gene SEQ ID Nos: 54 and 56 are recognized divergent subject matter. In addition, the different nucleic acids and amino acids are distinct because their structures are different and are therefore capable of separate manufacture, use and sale. Therefore the products of SEQ ID NO: 54 and 56, and a fusion protein comprising a portion of the gene of SEQ ID NO: 54 and 56 are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

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4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: It does not identify the mailing or post office address of each inventor. A mailing or post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing or post office address should include the ZIP Code designation. The mailing or post office address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

5. Claims 27-30 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

6. Claims 10-23 are under examination as they read on a nucleic acid segment of SEQ ID NO: 54, vectors and host cells.

7. The specification on page 1 should be amended to reflect the status of parent application No. 09/172,841 and 08/951,621.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 11-12, 16-17 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- A. The “recombinant host cell” recited in claim 22 has no antecedent basis in base claim 20. Base claim 21 only recites a host cell.
- B. The recitation of “standard hybridization conditions” in claim 11 is ambiguous. Although the specification discloses on page 22 general parameters for calculating such conditions, it is unclear which conditions are actually claimed.

It is suggested that Applicant amend the claims to recite a particular set of hybridization and wash conditions, such as those exemplified on page 22 of the specification, to overcome this rejection.

- C. Claims 11 and 16 are indefinite in the recitation of “at least one functionally active F-box domain”. It is unclear what functionally active domains are contemplated. It is unclear how many functionally active F-box domains are encoded by the nucleic acid segment.

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10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 11, 12 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The nucleic acid segment which is capable of hybridizing to the nucleotide sequence of SEQ ID NO: 54 under "standard" hybridization conditions claimed in claim 11 and the nucleic acid segment which defined further as "consisting essentially of" the nucleotide sequence of SEQ ID NO: 54 claimed in claim 12, and the nucleic acid segment comprising at least a "14 nucleotide sequence corresponding to, or complementary to, the nucleic acid sequence of SEQ ID NO: 54" claimed in claim 23 represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 07/30/02 does not point to the specification for support for the newly added limitations "standard", "consisting essentially of", and "14 nucleotide sequence corresponding to, or complementary to, the nucleic acid sequence of SEQ ID NO: 54" as claimed in claims 11, 12 and 23 respectively. However, the specification does not provide a clear support of "standard", "consisting essentially of", and "14 nucleotide sequence corresponding to, or complementary to, the nucleic acid sequence of SEQ ID NO: 54". The instant claims now claim limitations which were not clearly disclosed in the specification and claims as originally filed.

12. Claims 10-11 and 14-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleotide sequence of SEQ ID NO: 54 encoding SEQ ID NO: 53 for targeted ubiquitination; does not reasonably provide enablement for any nucleic acid segment comprising a nucleic acid sequence "substantially homologous" to the gene sequence of SEQ ID NO: 54 in claim 10, The nucleic acid segment further defined as encoding at least one functionally active F-box domain, wherein the segment is capable of hybridizing to the nucleotide sequence of SEQ ID NO: 54 under "standard hybridization conditions" in claim 11, the nucleic acid segment wherein said sequence further comprises 5' and 3' flanking regions in claim 14, wherein said gene further comprises intervening sequences in claim 15, a vector comprising any nucleic acid segment, wherein the nucleic acid segment is "substantially homologous to a portion" of the coding strand of the gene sequence set forth in SEQ ID NO: 54 in claim 18, or any nucleic acid segment comprising at least a 14 nucleotide sequence corresponding to, or complementary to, the nucleic acid sequence of SEQ ID NO: 54 in claim 23. The specification does not enable any person skilled in the art to which it pertains, or with

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which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses only a single nucleic acid sequence of SEQ ID NO:54 encoding a single polypeptide (human F2 beta) (SEQ ID NO:53) with a disclosed activity in targeted ubiquitination of cellular proteins (e.g., page 43-48). The instant claims encompass in their breadth *any* nucleic acid segment comprising a nucleic acid sequence substantially homologous to SEQ ID NO: 54; or *any* nucleic acid that hybridizes “under standard hybridization conditions”, including those that comprise a “portions” of SEQ ID NO: 54 (substantially homologous to a portion); or nucleic acids comprising “at least a 14 nucleotide sequence”. The nucleic acid segment further encompass “5’ and 3’ flanking regions” and “intervening sequences”.

There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various nucleic acids recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for targeted ubiquitination of cellular proteins. Without detailed direction as to which nucleic acid sequences are essential to the function of the encoded polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of nucleic acid sequences encompassed by the instant claims would share the ability to target cellular proteins for ubiquitination of the encoded polypeptide of SEQ ID NO:53, other than the nucleic acid of SEQ ID NO:54 encoding SEQ ID NO:53.

Attwood (Science 2000; 290:471-473) teaches that “[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., “Abstract” and “Sequence-based approaches to function prediction”, page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan’s best guess as to the function of the structurally related protein (see in particular “Abstract” and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

The skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity *over the full length of SEQ ID NO:53 to share the same function*. Thus the recitation of

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homologous language, in the absence of *a testable function* and limitations regarding the *sequence length over which the percent identity is required*; does not allow the skilled artisan to make and use the encoding nucleic acids commensurate in scope with the instant claims without undue experimentation.

The fact that two nucleic acid sequences will hybridize under moderate or stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus the same observations apply to the recitation of “a nucleic acid that hybridizes under standard hybridization conditions” as were noted above with respect to “homologous” language. Further, it was well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability *with respect to the full-length nucleic acid* is possible. In the absence of a clear recitation that the identity is over the full length of SEQ ID NO:54 the claim reads on subsequences. Finally, hybridization under conditions other than high stringency would be expected to permit a great deal of variation between the two hybridizing sequences, making it even more unpredictable that the two sequences would share the same function. Thus as for the recitation of hybridization language in the absence of *a testable function* and limitations regarding both the *hybridization conditions* and the *sequence length over which the hybridization takes place*; does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

The term “comprising” in claims 10, 18, and 23 is open-ended, means that a nucleic acid may include additional nucleic acids on either or both of the 5' or 3' termini of given sequence such as *the substantially homologous gene, the 14 nucleotide sequence or the homologous to a portion*. The instant claim language appears to encompass portions. For example, claims 18 and 23 recite *a nucleic acid segment is substantially homologous to a portion and a nucleic acid segment comprising at least a 14 nucleotide sequence*, respectively. Such a recitation does not require that the nucleic acid encode the full length sequence set forth in SEQ ID NO:54; but rather encompasses any nucleic acid sequence comprising either the full length of SEQ ID NO:54 or *any fragment*. However, the specification does not appear to have provided sufficient guidance as to which fragments of SEQ ID NO:54 would share the function of targeted ubiquitination. Neither does the specification appear to have provided any working examples of any functional fragments. Thus it would require undue experimentation of the skilled artisan to determine which fragments of SEQ ID NO:54 would have the function of the full length molecule.

The specification does not appear to provide any 5' and 3' flanking regions or intervening sequences, therefore, the skill in the art would not know what nucleic acid sequences are claimed.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited nucleic acid sequences and still encode a polypeptide that maintains the functional properties of the polypeptide of SEQ ID NO:53 is unpredictable, as is the identity of which subsequences

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would encode a functional polypeptide; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

13. Claims 10-11 and 14-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of the nucleic acid segment of SEQ ID NO: 54 encoding amino acid of SEQ ID NO:53 for targeted ubiquitination of cellular protein.

Applicant is not in possession of any nucleic acid segment comprising a nucleic acid sequence "substantially homologous" to the gene sequence of SEQ ID NO: 54 in claim 10, The nucleic acid segment further defined as encoding at least one functionally active F-box domain, wherein the segment (b) is capable of hybridizing to the nucleotide sequence of SEQ ID NO:54 under "standard hybridization conditions in claim 11, the nucleic acid segment wherein said sequence further comprises 5' and 3' flanking regions in claim 14, wherein said gene further comprises intervening sequences in claim 15, a vector comprising any nucleic acid segment, wherein the nucleic acid segment is "substantially homologous to a portion" of the coding strand of the gene sequence set forth in SEQ ID NO: 54 in claim 18, or any nucleic acid segment comprising at least a 14 nucleotide sequence corresponding to, or complementary to, the nucleic acid sequence of SEQ ID NO: 54 in claim 23.

Applicant has disclosed only nucleic acid of SEQ ID NO: 53; therefore, the skilled artisan cannot envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

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Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 10, 14, 18-21 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier *et al* (GenBank Accession No. H58848, 1995).

Hillier *et al* teach a 419 nucleic acid segment comprising a nucleic acid sequence substantially homologous to the gene sequence of SEQ ID NO: 54. Further, Hillier *et al* teach pT7T3D vector and DH10B prokaryotic host cell comprising a 419 nucleic acid segment that is 98.5% identical to a portion of SEQ ID NO: 54, wherein the nucleic acid segment is substantially homologous to a portion of the coding strand at nucleic acid positions (21-409) of SEQ ID NO: 54 (see sequence alignment in particular). Hillier *et al* further teach a nucleic acid segment comprising 269 nucleotide sequence corresponding to nucleic acid 21-356 of SEQ ID NO: 54 (see sequence alignment in particular). The term “comprising” in instant claim 23 is open ended, it would open up the claim to include the reference 419 nucleic acid sequence.

Claim 10 is included because upon reading the claim in light of the specification page 22 lines 3-6, wherein the “substantially homologous” refers to any probe which can hybridize to single-stranded nucleic acid sequence. Thus, the 419 nucleic acid sequence is considered substantially homologous to the gene sequence in SEQ ID NO: 54.

Claim 14 is included because Hillier *et al* teach the 419 nucleic acid sequence in a vector, which contain 5' regulatory sequences and 3' termination of transcription sequence.

The reference teachings anticipate the claimed invention.

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16. Claims 10-11, 14, 18-21 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier *et al* (GenBank Accession No. H58795, 1995).

Hillier *et al* teach a 339 nucleic acid segment comprising a nucleic acid sequence substantially homologous to the gene sequence of SEQ ID NO: 54, wherein the segment is capable of hybridizing to the nucleotide sequence of SEQ ID NO: 54 under standard hybridization conditions. Further, Hillier *et al* teach pT7T3D vector and DH10B prokaryotic host cell comprising a 339 nucleic acid segment that is 100% identical to a portion of SEQ ID NO: 54, wherein the nucleic acid segment is substantially homologous to a portion of the coding strand at nucleic acid positions (1161-1271) of SEQ ID NO: 54 (see sequence alignment in particular). Hillier *et al* further teach a nucleic acid segment comprising 111 nucleotide sequence complementary to nucleic acid 1161-1271 of SEQ ID NO: 54 (see sequence alignment in particular). The term "comprising" in instant claims 18 and 23 is open ended, it would open up the claim to include the reference 339 nucleic acid sequence.

Claims 10-11 are included because upon reading the claims in light of the specification page 22 lines 3-6, wherein the "substantially homologous" refers to any probe which can hybridize to single-stranded nucleic acid sequence. Therefore, the 339 nucleic acid sequence is considered substantially homologous to the gene sequence in SEQ ID NO: 54.

Claim 14 is included because Hillier *et al* teach the 419 nucleic acid in a vector which contain 5' regulatory sequences and 3' termination of transcription sequence.

The reference teachings anticipate the claimed invention.

17. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier *et al* (GenBank Accession No. H58848, 1995) or Hillier *et al* (GenBank Accession No. H58795, 1995) each in view of Darnell *et al*.

The teachings of Hillier *et al* (GenBank Accession No. H58848, 1995) or Hillier *et al* (GenBank Accession No. H58795, 1995) references have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of a eukaryotic host cell in claim 22.

Darnell *et al* teach that in order to prepare an unlimited amount of a pure gene, a vector containing the gene can be grown in a host cell and DNA extracted. Darnell *et al* also teach an expression vector in order to take advantage of "bacterial tricks" that increase mRNA synthesis to produce large quantities of desired proteins using a eukaryotic vector and host cell, or a prokaryotic and bacterial vector and host cell (page 255-258 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to express the DNA taught by the Hillier *et al* (GenBank Accession No. H58848, 1995) and

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Hillier *et al* (GenBank Accession No. H58795, 1995) references using the eukaryotic host cells as taught by Darnell *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because a eukaryotic host cell containing the a gene offers to prepare an unlimited amount of a pure gene as well as to produce large quantities of desired proteins as taught by Darnell *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. It appears that the nucleic acid of SEQ ID NO: 54 encoding SEQ ID NO:53 is free from prior art.

19. Claim 13 is objected to as being dependent upon a rejected base claim 10, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
January 10, 2003


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600